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HEDMAN & COSTIGAN, P.C.
1230 AVENUE OF THE AMERICAS
7th floor
NEW YORK, NY 10020

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CLAYTOR, DEIRDRE RENEE	
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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte MAXWELL GORDON

Appeal 2010-007607
Application 10/762,714
Technology Center 1600

Before DEMETRA J. MILLS, LORA M. GREEN, and
JEFFREY N. FREDMAN, *Administrative Patent Judges.*

FREDMAN, *Administrative Patent Judge.*

DECISION ON APPEAL[1]

This is an appeal under 35 U.S.C. § 134 involving claims to a pharmaceutical dosage form. The Examiner rejected the claims as obvious. We have jurisdiction under 35 U.S.C. § 6(b). We affirm.

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[1] The two-month time period for filing an appeal or commencing a civil action, as recited in 37 C.F.R. § 1.304, or for filing a request for rehearing, as recited in 37 C.F.R. § 41.52, begins to run from the "MAIL DATE" (paper delivery mode) or the "NOTIFICATION DATE" (electronic delivery mode) shown on the PTOL-90A cover letter attached to this decision.

Statement of the Case

The Specification teaches that the "invention relates to solid dosage forms of oral analgetic drugs which are effective for pain control(or treating diarrhea) and are not adapted for recovery of the opiate analgetic" (Spec. 1, ll. 17-20).

The Claims

Claims 1-6, 16-18, 21 and 22 are on appeal. Claims 1, 6, and 16 are representative. Claims 1, 6, and 16 read as follows:

> 1. A solid pharmaceutical dosage form which comprises an opiate, an opiate antagonist and an amount of hydrocolloids and other excipients including starch, lactose, xanthan gum, locust bean gum, monobasic calcium phosphate, dibasic calcium phosphate, microcrystalline cellulose, propylene glycol alginate, zein and magnesium stearate which are effective to form a viscous, non-injectable matrix when said dosage form is contacted with water.
>
> 6. A solid pharmaceutical dosage form as defined in claim 1 which includes an amount of enteric coated opiate antagonist pellets which is effective to reduce or eliminate the constipating effects of oycodone, methadone, morphine, codeine, dilaudid, pantopon, paregoric, pentazocine, buprenorphine, fentanyl, oxymorphone, hydromorphone, hydrocodone, propoxyphene, nalbuphine and meperidine.
>
> 16. A solid pharmaceutical dosage form which comprises a controlled release dosage form of an opiate, an opiate antagonist and a hydrocolloid and excipients as defined in claim 1, wherein said opiate, an opiate antagonist, hydrocolloid and

> excipients are formulated into pellets (a); pellets (b) and pellets (c) ;
>
> pellets (a) comprise about one-third of said opiate, opiate antagonist and hydrocolloid in an immediate release form;
>
> pellets (b) comprise about one-third of said opiate, opiate antagonist, hydrocolloid and excipients in an a delayed release form which releases substantially all contents of the pellets in the jejunum; and
>
> pellets (c) comprise about one-third of said opiate, opiate antagonist, hydrocolloid and excipients in a delayed release form which substantially all of the contents of the pellets in the ileum.

The issue

The Examiner rejected claims 1-6, 16-18, 21, and 22 under 35 U.S.C. § 103(a) as obvious over Oshlack[2] and Meissner[3] (Ans. 3-5).

The Examiner finds that "Oshlack et al. teach solid dosage forms of compositions comprised of an opiate, an opiate antagonist and a hydrocolloid containing excipient" (Ans. 3). The Examiner finds that "Meissner et al. teaches improved laxation during oral naloxone treatment in opioid-associated constipation" (Ans. 5). The Examiner finds it obvious "to formulate a composition comprised of an opiate, an opiate antagonist, hydrocolloids and other excipients as exemplified in claim 1 because Oshlack et al. teach the suitability of all of the hydrocolloids and excipients

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[2] Oshlack et al., US 7,144,587 B2, issued Dec. 5, 2006.
[3] Meissner et al., *Oral naloxone reverses opioid-associated constipation*, 84 PAIN 105-109 (2000).

in a composition of coated beads with an opiate and an opiate antagonist" (Ans. 5).

Appellant contends that it "is not seen how a reference can make obvious a formulation having ingredients that are not disclosed by the reference. Oshlack teaches the use of sequestered aversive agents that impart a bitter, irritant or gelling effect when the dosage form is not used for its intended use" (App. Br. 4). Appellant argues that an "opiate antagonist that is sequestered or non-available may be added to the Oshlack teachings but such a sequestered agent can have no role in reducing or prevent constipation according to composition claim 6 and method claim 22 which both utilize an enteric" (App. Br. 4-5).

Appellant contends that "[c]laim 16 points out a specific three pellet formulation where the pellets are formulated to release the drugs in specific anatomical locations of the small intestine. This formulation is also not made obvious by Oshlack and/or Meissner" (App. Br. 5).

The issue with respect to this rejection is: Does the evidence of record support the Examiner's conclusion that Oshlack and Meissner render obvious the claimed solid pharmaceutical dosage forms?

Findings of Fact

1. Oshlack teaches "preventing or deterring of the abuse of opioid analgesics by the inclusion of an opioid antagonist and at least one aversive agent in the dosage form with the opioid analgesic" (Oshlack, col. 6, ll. 17-20).

2. Oshlack teaches that "various gelling agents can be employed including . . . starch and starch derivatives, cellulose derivatives, such as

microcrystalline cellulose, . . . xanthan gum, . . . polyethylene glycol, . . . mixed surfactant/wetting agent systems, emulsifiers, other polymeric materials, and mixtures thereof" (Oshlack, col. 7, ll. 23-36).

3. Oshlack teaches that when "being formulated as a tablet, the aversive agent and opioid agonist and opioid antagonist may be combined with one or more inert, non-toxic pharmaceutical excipients which are suitable for the manufacture of tablets. Such excipients include, for example, an inert diluent such as lactose" (Oshlack, col. 16, ll. 50-55).

4. Oshlack teaches that "[o]ther gelling agents such as . . . alginates . . . locust bean gum . . . could also be used as gelling agents" (Oshlack, col. 35, ll. 26-32).

5. Oshlack teaches a formulation in Example 6 which comprises dicalcium phosphate (*see* Oshlack, Example 6, col. 39, l. 34).

6. Oshlack teaches that in "certain embodiments of the dosage forms of the present invention may also include a surfactant. Surfactants useful in accordance with the present invention, include for example . . . propylene glycol" (Oshlack, col. 32, ll. 48-65).

7. Oshlack teaches that in "certain embodiments, a sustained release coating is applied to the sustained release spheroids, granules, or matrix multiparticulates. In such embodiments, the sustained-release coating may include . . . zein" (Oshlack, col. 25, ll. 4-9).

8. Oshlack teaches a formulation in Example 1 which comprises magnesium stearate (*see* Oshlack, Example 1, col. 35, l. 50).

9. Oshlack teaches that the "aversive agent can be combined with an enteric carrier to delay its release or combined with a carrier to provide a

sustained release of the aversive agent" (Oshlack, col. 4, ll. 12-15). Oshlack also teaches that "the antagonist . . . can be an antagonist with minimal oral activity such as naloxone in releasable or 'non-sequestered' form" (Oshlack, col. 4, ll. 35-37).

10. Oshlack teaches that the formulation "can be formulated as an immediate release formulation or controlled release oral formulation in any suitable tablet, coated tablet or multiparticulate formulation known to those skilled in the art" (Oshlack, col. 17, ll. 12-17).

11. The Examiner finds that "the teaching of dicalcium phosphate renders the monocalcium phosphate obvious because the compounds are similar and have similar properties of being excipients" (Ans. 4)).

12. Meissner teaches that "[o]pioid-related constipation is one of the most frequent side effects in chronic pain patients, sometimes to the extent that treatment with morphine and other opioids must be reduced" (Meissner 105, col. 1).

13. Meissner teaches that "[p]atients preferred naloxone to the previously used laxatives because of the stronger effect, the rapid onset of laxation, and the unpleasant taste of lactulose" (Meissner 108, col. 2).

Principles of Law

"The combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results." *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 416 (2007). "If a person of ordinary skill can implement a predictable variation, § 103 likely bars its patentability." *Id.* at 417. Moreover, an "[e]xpress suggestion to substitute one equivalent for another need not be present to render such substitution

obvious." *In re Fout*, 675 F.2d 297, 301 (CCPA 1982). As noted by the Court in *KSR*, "[a] person of ordinary skill is also a person of ordinary creativity, not an automaton." 550 U.S. at 421.

Analysis

Claim 1

Oshlack teaches "preventing or deterring of the abuse of opioid analgesics by the inclusion of an opioid antagonist and at least one aversive agent in the dosage form with the opioid analgesic" (Oshlack, col. 6, ll. 17-20; FF 1). Meissner teaches that "[o]pioid-related constipation is one of the most frequent side effects in chronic pain patients, sometimes to the extent that treatment with morphine and other opioids must be reduced" (Meissner 105, col. 1; FF 12). Meissner teaches that "[p]atients preferred naloxone to the previously used laxatives because of the stronger effect, the rapid onset of laxation, and the unpleasant taste of lactulose" (Meissner 108, col. 2; FF 13).

Applying the *KSR* standard of obviousness to the findings of fact, we conclude that the person of ordinary creativity would have predictably incorporate naloxone into the opioid analgesic of Oshlack to reduce any opioid related constipation taught as a problem by Meissner (FF 12-13). Further, the ordinary practitioner would have used components taught or rendered obvious by Oshlack for the composition (FF 1-8, 11). Such a combination is merely a "predictable use of prior art elements according to their established functions." *KSR*, 550 U.S. at 417.

Appellant contends that it "is not seen how a reference can make obvious a formulation having ingredients that are not disclosed by the

reference. Oshlack teaches the use of sequestered aversive agents that impart a bitter, irritant or gelling effect when the dosage form is not used for its intended use" (App. Br. 4).

We are not persuaded. Oshlack teaches, or renders obvious, each of the components of Claim 1 for use in opioid compositions, specifically teaching the use of starch (FF 2), lactose (FF 3), xanthum gum (FF 2), locust bean gum (FF 4), monobasic calcium phosphate (FF 11), dibasic calcium phosphate (FF 5), microcrystalline cellulose (FF 2), propylene glycol (FF 6), alginate (FF 4), zein (FF 7) and magnesium stearate (FF 8).

While we are fully aware that hindsight bias often plagues determinations of obviousness, *Graham v. John Deere Co.*, 383 U.S. at 36, we are also mindful that the Supreme Court has clearly stated that the "combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results," *KSR*, 550 U.S. at 401. This reasoning is applicable, since the instant invention simply combines components taught or rendered obvious by Oshlack and Meissner for their predictable functions (FF 1-13). Appellant has provided no evidence of any secondary consideration (*see* App. Br. 4-5).

Claims 6 and 22

Appellant argues that an "opiate antagonist that is sequestered or non-available may be added to the Oshlack teachings but such a sequestered agent can have no role in reducing or prevent constipation according to composition claim 6 and method claim 22 which both utilize an enteric" (App. Br. 4-5).

We are not persuaded. Oshlack specifically teaches that the "aversive agent can be combined with an enteric carrier to delay its release or combined with a carrier to provide a sustained release of the aversive agent" (Oshlack, col. 4, ll. 12-15; FF 9). Oshlack also teaches that in "certain embodiments, a sustained release coating is applied to the sustained release spheroids, granules, or matrix multiparticulates. In such embodiments, the sustained-release coating may include . . . zein" (Oshlack, col. 25, ll. 4-9; FF 7). We also agree with the Examiner that "Oshlack teaches that the antagonist can be in a sequestered form as well as a non-sequestered form (see Col. 4, lines 35-45). Therefore, an antagonist such as naloxone will be available to reduce constipation" (Ans. 6; *see* FF 4).

Claim 16

Appellant argues that "[c]laim 16 points out a specific three pellet formulation where the pellets are formulated to release the drugs in specific anatomical locations of the small intestine. This formulation is also not made obvious by Oshlack and/or Meissner" (App. Br. 5).

We are not persuaded. Oshlack teaches that the formulation "can be formulated as an immediate release formulation or controlled release oral formulation in any suitable tablet, coated tablet or multiparticulate formulation known to those skilled in the art" (Oshlack, col. 17, ll. 12-17; FF 10). Thus, Oshlack specifically suggests multiparticulate formulations which may be composed of immediate and controlled release particles (FF 10). Appellant does not explain why claim 16 would have been unobvious over Oshlack's teaching by showing some unobvious result or secondary consideration.

Conclusion of Law

The evidence of record support the Examiner's conclusion that Oshlack and Meissner render obvious the claimed solid pharmaceutical dosage forms.

SUMMARY

In summary, we affirm the rejection of claims 1, 6, 16, and 22 under 35 U.S.C. § 103(a) over Oshlack and Meissner. Pursuant to 37 C.F.R. § 41.37(c)(1)(vii)(2006), we also affirm the rejection of claims 1-5, 17, 18, and 21, as these claims were not argued separately.

No time period for taking any subsequent action in connection with this appeal may be extended under 37 C.F.R. § 1.136(a)(1)(iv)(2006).

AFFIRMED

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HEDMAN & COSTIGAN, P.C.
1230 AVENUE OF THE AMERICAS
7th floor
NEW YORK NY 10020